

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

**THIS PAGE BLANK (USPTO)**

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : A61L 27/58, 27/42, 27/46, 31/14, 31/12		A1	(11) International Publication Number: WO 00/47245 (43) International Publication Date: 17 August 2000 (17.08.00)
(21) International Application Number: PCT/GB00/00475 (22) International Filing Date: 11 February 2000 (11.02.00) (30) Priority Data: 9902976.1 11 February 1999 (11.02.99) GB (71) Applicant (for all designated States except US): GILTECH LIMITED [GB/GB]; 9/12 North Harbour Estate, Ayr KA8 8BN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): HEALY, David, Michael [IE/GB]; Midton House, By Alloway, Ayr KA7 4EG (GB). GILCHRIST, Thomas [GB/GB]; The Lodge, 67 Midton Road, Ayr KA7 2TW (GB). (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
(54) Title: BIODEGRADABLE COMPOSITE MATERIAL FOR TISSUE REPAIR			
(57) Abstract <p>There is described a biodegradable composite material for tissue repair comprising a water-soluble glass, preferably as glass fibres and/or particles in the form of a matrix, impregnated with a biodegradable polymer. An especially preferred polymer is poly <math>\epsilon</math>-caprolactone. The biodegradable composite is particularly useful for the repair of nerve and/or bone tissue, especially the bones of the skull. A method of producing the composite material is also described.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

1     **Biodegradable Composite Material for Tissue Repair**

2

3     The present invention relates to a composite material  
4     which is especially useful in bone repair.

5

6     Most commonly defects to bone arise from injury, but  
7     may also be due to congenital abnormalities, to  
8     acquired deformity or to ablation of tumours. Without  
9     adequate repair, bone defects can significantly affect  
10    function of the associated limb, and frequently the  
11    mobility of the patient is impaired. Where the bone  
12    defect is present in the skull, there may be cosmetic  
13    considerations and without adequate repair the  
14    appearance of the patient may be adversely affected.

15

16    Repair and reconstruction of defective bone currently  
17    involves either the use of auto-graft tissue (ie where  
18    bone is removed from another part of the patient's body  
19    and used for repair) or the use of bio-compatible  
20    materials. Allograft bone transplants (ie using  
21    donated bone material) are still the main source of  
22    material for bone repair, despite the risk of disease  
23    transmission, notably HIV or CJD, due to contaminated  
24    sources. Both of the current approaches also suffer  
25    other disadvantages: the need to obtain bone from the

1 patient for use in the auto-graft requires further  
2 invasive procedure(s) and a second wound site in the  
3 patient; and the bio-compatible materials currently  
4 available are not suitable for all types of bone repair  
5 and are particularly inadequate for repairing defects  
6 of the skull.

7  
8 The present invention provides a biodegradable  
9 composite material suitable for implantation in a  
10 patient's body, said composite material comprising  
11 water-soluble glass and a biodegradable polymer.

12  
13 The water-soluble glass material may be in the form of  
14 fibres, particles or mixtures thereof. As used herein  
15 the term "glass fibres" refers to glass in both wool  
16 and mono-filament form. The length of the fibres is  
17 not critical and would normally be chosen to suit the  
18 size of composite required.

19  
20 Examples of suitable water-soluble glass fibres include  
21 the fibres described in WO-A-98/54104, WO-A-99/62834  
22 and WO-A-99/62835 (all in the name of Giltech Limited),  
23 the content of each of these publications being  
24 incorporated herein by reference.

25  
26 The biodegradable polymer may be any suitable bio-  
27 compatible polymer or mixtures of such polymers.  
28 Preferably the polymer exhibits some pliability or  
29 plasticity. Examples include (but are not limited to)  
30 polyvinyl alcohols, polysaccharides (for example  
31 alginates and chitosan), polyglycolic acid, polylactic  
32 acid, polyglycolactide, polyhydroxybutyrate,  
33 polyhydroxyvalerate, polycaprolactones (for example  
34 poly  $\epsilon$ -caprolactone), polycaprolactam and starches  
35 (especially "thermoplastic" starches such as  
36 hydroxypropylated starches, or potato, maize or rice

1 starch treated by high pressure and humidity). Co-  
2 polymers of these polymers may also be used (for  
3 example polyglycolide (or polyglycolic acid)/  
4 polycaprolactone co-polymer or a polyglycolic  
5 acid/polycaprolactam co-polymer).  
6

7 A preferred biodegradable polymer is poly( $\epsilon$ -  
8 caprolactone), or any other slowly degrading polymer  
9 material.  
10

11 In one embodiment, the water-soluble glass material  
12 will degrade more slowly (and usually at a  
13 significantly slower rate) than the biodegradable  
14 polymer. Alternatively, the biodegradable polymer will  
15 degrade more slowly than the water-soluble glass  
16 material.  
17

18 Advantageously the glass material, in addition to  
19 contributing to the strength of the composite material,  
20 will provide a suitable environment for initiation of  
21 bone repair. Desirably therefore osteoblasts are able  
22 to penetrate the biodegradable polymer in order to  
23 attach to the glass material and commence bone  
24 formation. Generally the size of the glass material  
25 will be selected to degrade in a time-scale comparable  
26 to bone repair.  
27

28 The polymer provides a sponge-like environment around  
29 the water-soluble glass, and becomes wetted by body  
30 fluids when the composite material is placed in the  
31 body. Where water-soluble glass particles or fibres  
32 are present in the composite, slight dissolution of  
33 polymer occurs around the sites where the glass is  
34 present and may cause a general loosening of the  
35 composite. The degree of loosening may be beneficial  
36 in some embodiments since the areas created are

1 available for tissue ingrowth. Loss of mechanical  
2 strength in the composite material may be countered by  
3 including randomly orientated fibres and/or the release  
4 of zinc ions from the glass, which would promote cross-  
5 linking and repolymerisation of the polymer (especially  
6 poly  $\epsilon$ -caprolactone) around the glass.

7  
8 A further advantage of the composite described is that  
9 it is mouldable, and it may be contoured to fit the  
10 implant site closely.

11  
12 The composite material may comprise a matrix of water-  
13 soluble glass material, the matrix being impregnated  
14 with the biodegradable polymer. Optionally the glass  
15 material (fibres and/or particles) is arranged to  
16 provide adequate strength in the load-bearing  
17 dimensions of the composite.

18  
19 In a further aspect the present invention provides a  
20 method of repairing an area of defective tissue (for  
21 example nerve or bone) in a patient, said method  
22 comprising implanting a composite material as described  
23 above into said patient in sufficient quantity to cover  
24 and/or fill said area. Optionally said composite  
25 material is attached to healthy tissue using  
26 conventional (preferably biodegradable) means. Mention  
27 may be of sutures and biodegradable glue in this  
28 respect.

29  
30 The biodegradable composite of the present invention  
31 may be used to form pins, plates, nuts or bolts to hold  
32 shattered bone pieces together, or may be formed into  
33 flexible sheet form to wrap around a defective tissue.

34  
35 In a further aspect, the present invention provides a  
36 method of producing a composite material suitable for



1 tissue repair, said method comprising:

2

3 a) providing water-soluble glass fibres and/or  
4 glass particles;

5 b) optionally arranging said fibres and/or  
6 particles into a pre-selected order;

7 c) covering said fibres and/or particles with a  
8 biodegradable polymer and if required allowing  
9 said polymer to cure.

10

11 In one embodiment the composite material may be formed  
12 using liquid moulding techniques. For example the  
13 required array of glass fibres and/or particles may be  
14 positioned in a closed mould cavity into which the  
15 polymer is then introduced. A rigid composite material  
16 is formed once the polymer has cured. Optionally  
17 introduction of the polymer into the mould may be  
18 vacuum assisted.

19

20 Where poly( $\epsilon$ -caprolactone) is used as the polymer,  
21 conducting the polymerisation reaction within the mould  
22 cavity itself may be desirable since introduction of  
23 this polymer into the mould is difficult due to the  
24 high viscosity of poly( $\epsilon$ -caprolactone). A ring-opening  
25 polymerisation of caprolactone using 1,4-butanediol  
26 catalyzed with diethylzinc may be suitable for such in  
27 situ polymerisation.

28

29 Alternatively, a suitable composite material may be  
30 produced by forming glass fibre into a glass fibre  
31 fabric which can then be simply dipped into the plastic  
32 polymer. Alternatively, the polymer may be sprayed  
33 onto the fibre. In addition to the techniques of  
34 thermoforming and weaving, the glass fibres could also  
35 be spun into a yarn, the fibres or yarn being  
36 optionally knitted, braided or crocheted. Likewise

1 where glass wool is used, the wool may be shaped as  
2 required and either dipped into the plastic polymer or  
3 placed into a closed mould cavity for liquid moulding  
4 as described above.

5

6 In a further embodiment glass particles are used  
7 together with short lengths of glass fibres.

8

9 In a yet further aspect, the present invention provides  
10 the use of a composite material as described above for  
11 repairing damaged or defective tissue (especially bone  
12 or nerve tissue) in a body.

13

14 Desirably the composite material is sterilised prior to  
15 implantation in the body, for example by irradiation.

16

17 Phosphorous pentoxide ( $P_2O_5$ ) is preferably used as the  
18 glass former.

19

20 Generally the mole percentage of phosphorous pentoxide  
21 in the glass composition is less than 85%, preferably  
22 less than 60% and especially between 30-60%.

23

24 Alkali metals, alkaline earth metals and lanthanoid  
25 oxides or carbonates are preferably used as glass  
26 modifiers.

27

28 Generally, the mole percentage of alkali metals,  
29 alkaline earth metals and lanthanoid oxides or  
30 carbonates is less than 60%, preferably between 40-60%.

31

32 Boron containing compounds (eg  $B_2O_3$ ) are preferably used  
33 as glass additives.

34

35 Generally, the mole percentage of boron containing  
36 compounds is less than 15% or less, preferably less

1     than 10%, and usually around 5% or less.

2  
3     Other compounds may also be added to the glass to  
4     modify its properties, for example  $\text{SiO}_2$ ,  $\text{Al}_2\text{O}_3$ ,  $\text{SO}_3$  or  
5     transition metal compounds (eg. first row transition  
6     metal compounds). Generally, the glass will release  
7     ionic species upon dissolution, the exact ionic species  
8     released depending upon the compounds added to the  
9     glass. Glasses which release aluminium ions, sulphate  
10    ions or fluorine ions may be desirable in some  
11    circumstances.

12  
13    Typically the soluble glasses used in this invention  
14    comprise phosphorus pentoxide ( $\text{P}_2\text{O}_5$ ) as the principal  
15    glass-former, together with any one or more  
16    glass-modifying non-toxic materials such as sodium  
17    oxide ( $\text{Na}_2\text{O}$ ), potassium oxide ( $\text{K}_2\text{O}$ ), magnesium oxide  
18    ( $\text{MgO}$ ), zinc oxide ( $\text{ZnO}$ ) and calcium oxide ( $\text{CaO}$ ). The  
19    rate at which the glass dissolves in fluids is  
20    determined by the glass composition, generally by the  
21    ratio of glass-modifier to glass-former and by the  
22    relative proportions of the glass-modifiers in the  
23    glass. By suitable adjustment of the glass  
24    composition, the dissolution rates in water at  $38^\circ\text{C}$   
25    ranging from substantially zero to  $25\text{mg}/\text{cm}^2/\text{hour}$  or more  
26    can be designed. However, the most desirable  
27    dissolution rate  $R$  of the glass is between 0.01 and  
28     $2.0\text{mg}/\text{cm}^2/\text{hour}$ .

29  
30    The water-soluble glass is preferably a phosphate  
31    glass, and may comprise a source of silver ions  
32    which may advantageously be introduced during  
33    manufacture as silver orthophosphate ( $\text{Ag}_3\text{PO}_4$ ). Other  
34    metals may alternatively or additionally be present and  
35    mention may be made of Cu, Mg, Zn, Ce, Mn, Bi, Se, Cs.  
36    Preferred metals include Ag, Cu, Zn and Mg. The glass

1 preferably enables controlled release of metal and  
2 other constituents in the glass and the content of  
3 these additives can vary in accordance with conditions  
4 of use and desired rates of release, the content of  
5 metal generally being up to 5 mole %. While we are  
6 following convention in describing the composition of  
7 the glass in terms of the mole % of oxides, of halides  
8 and of sulphate ions, this is not intended to imply  
9 that such chemical species are present in the glass nor  
10 that they are used for the batch for the preparation of  
11 the glass.

12  
13 The optimum rate of release of metal ions into an  
14 aqueous environment may be selected by circumstances  
15 and particularly by the specific function of the  
16 released metal. The invention provides a means of  
17 delivering metal ions to an aqueous medium at a rate  
18 which will maintain a concentration of metal ions in  
19 said aqueous medium of not less than 0.01 parts per  
20 million and not greater than 10 parts per million. In  
21 some cases, the required rate of release may be such  
22 that all of the metal added to the system is released  
23 in a short period of hours or days and in other  
24 applications it may be that the total metal be released  
25 slowly at a substantially uniform rate over a period  
26 extending to months or even years. In particular cases  
27 there may be additional requirements, for example it  
28 may be desirable that no residue remains after the  
29 source of the metal ions is exhausted or, in other  
30 cases, where the metal is made available it will be  
31 desirable that any materials, other than the metal  
32 itself, which are simultaneously released should be  
33 physiologically harmless. In yet other cases, it may  
34 be necessary to ensure that the pH of the resulting  
35 solution does not fall outside defined limits.

36

1 Generally, the mole percentage of these additives in  
2 the glass is less than 25%, preferably less than 10%.

3  
4 Embodiments of the invention will be described with  
5 reference to the following non-limiting examples.

6  
7 **Example 1**

8  
9 Method of forming a glass fibre

10  
11 The glass-forming composition is initially heated to a  
12 melting temperature of 500°-1200°C, preferably 750°-  
13 1050°C. The temperature is then slowly lowered to the  
14 working temperature at which fibre formation occurs.

15  
16 Generally, the working temperature of the glass will be  
17 at least 200°C lower than the temperature at which the  
18 glass is initially heated. Suitable working  
19 temperatures may fall within the following ranges 400°-  
20 500°C, 500°-900°C (preferably 550°-700°C, more  
21 preferably 550°-650°C, especially 600°-650°C) and 800-  
22 1000°C. The working temperature selected will depend  
23 upon the glass composition, but an approximate  
24 indication of a suitable working temperature can be  
25 established as hereinafter described. Depending upon  
26 the glass composition used, the working temperature may  
27 be a range of suitable temperatures. The range of  
28 working temperatures may be narrow, for example of only  
29 10°C, so that fibre formation may occur only between  
30 the temperature of N°C to (N+10)°C. Other glass  
31 compositions may have a wider temperature range for the  
32 working temperature in which glass formation is  
33 possible.

34  
35 Alternatively, the working temperature of the glass may  
36 be defined as 50-300°C above the T<sub>g</sub> of the glass.

1 In order to obtain an approximate indication of the  
2 working temperature for any particular glass  
3 composition, the glass composition should be slowly  
4 heated to its melting point. As soon as the glass is  
5 molten, frequent attempts to pull the composition  
6 upwardly to form a fibre should be made, with the  
7 temperature of the composition being very gradually  
8 increased between attempts. The temperature range of  
9 the composition during which fibre formation is  
10 possible should be noted and used as a preliminary  
11 working temperature in the process of the invention.  
12

13 It will be clear to those skilled in the art that the  
14 pulling speed at which the fibre is drawn off can  
15 affect the choice of working temperature and the  
16 diameter of the fibre required. Where a fibre of  
17 relatively large diameter is required, the fibre tends  
18 to be pulled more slowly and the working temperature  
19 may need to be decreased slightly. Where a fibre of  
20 relatively small diameter is required (eg a glass  
21 wool), the fibres may be drawn at the much higher  
22 pulling speed and the working temperature may need to  
23 be increased (thus lowering the viscosity of the  
24 composition to accommodate the increased pulling  
25 speed). Selection of the exact working temperature in  
26 respect of any particular fibre size and composition  
27 will be a simple matter of routine evaluation of  
28 optimal process conditions.  
29

30 With reference to the "working temperature" of the  
31 glass, the skilled person will appreciate that the  
32 furnace temperature may differ considerably from the  
33 temperature of the glass itself and indeed there may be  
34 a significant temperature gradient in the glass.  
35 Ideally the "working temperature" will be the  
36 temperature of the glass as fibre formation (ie.

1 pulling) takes place. In many compositions however, it  
2 may not be practical to measure the temperature at the  
3 surface of the glass where pulling occurs by insertion  
4 of a temperature probe as the introduction of the probe  
5 may precipitate crystallisation of the glass. One  
6 alternative is to place a temperature probe into the  
7 bushing and to monitor the bushing temperature which  
8 will be a good indicator of the glass temperature at  
9 the moment of fibre formation. Alternatively an Infra  
10 Red pyrometer may be focused onto the appropriate area  
11 of the glass and used to monitor the temperature.

12  
13 The glass to be formed into fibres will generally be  
14 heated until molten, optionally clarified, and then  
15 cooled slowly and controllably until the appropriate  
16 working temperature is reached and fibre formation can  
17 commence. The initial heating of the glass above its  
18 melting point and the subsequent fibre formation may be  
19 carried out in a single vessel or, alternatively, the  
20 molten glass may be transferred to a vessel designed  
21 specifically for fibre formation. One way of holding  
22 the molten glass in a vessel having a bushing within  
23 its lower surface until the temperature drops to the  
24 required working temperature is to coat or fill the  
25 holes of the bushing with a material that gradually  
26 melts over the period of time taken for the glass to  
27 reach the temperature required.

28  
29 The most important aspect of the method is the manner  
30 in which the working temperature is reached. We have  
31 found that the molten glass, which may preferably be  
32 heated significantly above its melting point, should be  
33 allowed to cool in a highly controlled manner, the  
34 temperature being only gradually reduced until the  
35 working temperature is reached. A stirrer may be  
36 present to ensure that the temperature of the whole of



1 the molten glass is kept as uniform as possible.

2

3 The glass is cooled to a temperature at which the glass  
4 will not crystallise for at least the period of time  
5 needed to convert the melt to fibre. This temperature  
6 is termed herein as a "holding temperature". The rate  
7 of cooling from this holding temperature is determined  
8 by the rate at which the melt is consumed at the  
9 bushing and the difference in temperature between the  
10 bushing temperature (the working temperature) and the  
11 melt holding temperature.

12

13 Due to low viscosity and narrow temperature band for  
14 many of these compositions, control of the balance  
15 between melt temperature, bushing temperature and glass  
16 throughput rate is critical.

17

18 Examples 2 to 16 detail suitable compositions which can  
19 be formed into fibres using the method of Example 1.  
20 Alternatively, these glasses can be cast in a  
21 conventional way and used to form particles, powder or  
22 granules.

23

#### 24 Example 2

25

#### 26 Glass Composition

27

28

29

30

31

32

33

34 100 grams of the sample was heated to 900°C before  
35 being cooled and pulled at 650°C, at 25 km/hr. Overall  
36 the fibre was good; one sample was 10 km in length and



1 11 grams in weight, although there was some  
2 crystallisation at the pulling temperature.

3

4 **Example 3**

5	Component	Mole %
6	Glass Composition	
7	Na <sub>2</sub> O	29.51
8	CaO	15.21
9	Ag <sub>2</sub> O	3.68
10	P <sub>2</sub> O <sub>5</sub>	43.80
11	2Al <sub>2</sub> O <sub>3</sub> .B <sub>2</sub> O <sub>3</sub>	1.90
12	Na <sub>2</sub> PO <sub>3</sub> F	1.90
13	Na <sub>2</sub> B <sub>4</sub> O <sub>7</sub> .10H <sub>2</sub> O	1.00
14	Na <sub>2</sub> PO <sub>4</sub>	3.00

15

16 74 grams of the sample was heated to 1000°C before  
17 being cooled and pulled at 635°C at 25 km/hr. The  
18 fibre produced was ultrafine; one sample was 18 km in  
19 length and 59 grams in weight. The sample was sprayed  
20 with WD40 to prevent water absorption and to aid  
21 lubricity. There was some debris at the bottom of the  
22 crucible, but this was found to be just iron deposits  
23 from the brushing rod.

24

25 **Example 4**

26	Component	Mole %
27	Glass Composition	
28	Na <sub>2</sub> O	34.20
29	CaO	16.15
30	P <sub>2</sub> O <sub>5</sub>	44.65
31	Na <sub>2</sub> SO <sub>4</sub>	5.00

32

33 200 grams of the sample was heated to 1050°C before  
34 being cooled and pulled at 635°C at 25 km/hr. The  
35 fibre was good although there was some crystallisation  
36 at the pulling temperature.

1     **Example 5**

2		Component	Mole %
3	Glass Composition		
4		Na <sub>2</sub> O	32.40
5		CaO	15.30
6		P <sub>2</sub> O <sub>5</sub>	42.30
7		2Al <sub>2</sub> O <sub>3</sub> .B <sub>2</sub> O <sub>3</sub>	3.00
8		Na <sub>2</sub> PO <sub>3</sub> F	1.00
9		Na <sub>2</sub> SO <sub>4</sub>	6.00

10

11     117 grams of the sample was heated to 950°C before  
12     being cooled and pulled at 635°C, at 40 km/hr. The  
13     fibre produced was good and there were no  
14     crystallisation problems even though the surface  
15     temperature of the fibre dropped to 510°C in the  
16     pulling process.

17

18     **Example 6**

19		Component	Mole %
20	Glass Composition		
21		Na <sub>2</sub> O	31.71
22		CaO	14.73
23		P <sub>2</sub> O <sub>5</sub>	36.33
24		B <sub>2</sub> O <sub>3</sub>	4.78
25		SO <sub>3</sub>	9.40
26		Na <sub>2</sub> PO <sub>3</sub> F	3.00

27

28     99 grams of the sample was heated to 800°C before being  
29     cooled to 650°C and pulled at 40 km/hr. The fibre  
30     produced was very fine but difficult to pull and quite  
31     fragile at speed.

32

33

34

35

36

1     **Example 7**

2	Component	Mole %
3	Glass Composition	
4	Na <sub>2</sub> O	30.77
5	CaO	14.28
6	P <sub>2</sub> O <sub>5</sub>	35.28
7	B <sub>2</sub> O <sub>3</sub>	4.64
8	SO <sub>3</sub>	9.12
9	FePO <sub>4</sub>	2.41
10	Na <sub>2</sub> PO <sub>3</sub> F	0.20
11	Na <sub>2</sub> PO <sub>3</sub> F	0.20
12	MnHPO <sub>4</sub>	2.06

13  
14     200 grams of the sample was heated to 850°C before  
15     being cooled to 545°C and pulled at 40 km/hr. The  
16     fibre produced was strong and thin; there was not a  
17     problem of crystallisation, in fact the glass can be  
18     stored at 550°C for 72 hours without the onset of  
19     crystallisation.

20  
21     **Example 8**

22     Below is an example of a wool formulation and running  
23     conditions to illustrate the differences with the  
24     monofilament examples given above.

25  
26     A typical wool formulation is

27		
28	Na <sub>2</sub> O	26.31
29	CaO	17.78
30	P <sub>2</sub> O <sub>5</sub>	47.04
31	B <sub>2</sub> O <sub>3</sub>	5.94
32	MnO	1.55
33	Fe <sub>2</sub> O <sub>3</sub>	0.97
34	NaF	0.41

35  
36     Solution rate, non annealed = 0.0278 mg.cm<sup>2</sup>hr<sup>-1</sup>  
37     Melted and refined at 1000°C.  
38     Cooled and held at 725°C.  
39     Bushing temperature maintained at 365°C.

1 Thick fibres approx 1.2mm diameter drawn through pinch  
2 rollers at  $2.5 \text{ M.mm}^{-1}$  from a bushing with 6 x 6.5mm  
3 diameter holes. Fibres jet attenuated to produce a  
4 fine wool 5 -15 $\mu\text{m}$  diameter. The wool was sprayed with  
5 silicone oil finish during the attenuation process and  
6 collected on a stainless steel mesh conveyor.  
7 Typically, attenuated wools will have diameters of 5 to  
8 20 $\mu\text{m}$ . Monofilament fibres will mostly be 20 to 50 $\mu\text{m}$   
9 diameter.

10

11 **Example 9**

12	Na <sub>2</sub> O	31.19 mole %
13	K <sub>2</sub> O	9.63 mole %
14	Ag <sub>2</sub> O	2.9 mole %
15	B <sub>2</sub> O <sub>3</sub>	2.74 mole %
16	2NaF	0.66 mole %
17	P <sub>2</sub> O <sub>5</sub>	52.88 mole %

18 Furnace at 710°C - 800°C.

19 Bushing at 450°C - 460°C.

20 4.5mm bushing holes.

21 50km per hour pull rate.

22 Good fibres.

23 Solution rate = 1.68 not annealed 2.28 annealed.

24

25 **Example 10**

26	Na <sub>2</sub> O	32 mole %
27	K <sub>2</sub> O	10 mole %
28	Ag <sub>2</sub> O	3 mole %
29	P <sub>2</sub> O <sub>5</sub>	55 mole %

30

31 Furnace at 850°C.

32 Bushing at 530°C.

33 5mm bushing holes.

34 55kmph.

35 Good strong fibres.

36

37

38

39

1     **Example 11**

2	Na <sub>2</sub> O	32 mole %	
3	K <sub>2</sub> O	10 mole %	
4	(MgO	4 mole %)	- added as an anti-microbial
5	B <sub>2</sub> O <sub>3</sub>	5 mole %	
6	Ag <sub>2</sub> O	3 mole %	
7	P <sub>2</sub> O <sub>5</sub>	46 mole %	

8

9     Furnace temperature 650°C - 730°C.

10    Bushing temperature 410°C - 420°C.

11    Bushing 5.5mm diameter.

12    Speed up to 100kmph.

13    Solution rate 0.7 annealed 1.0 non annealed (mg.cm<sup>-3</sup>.hr<sup>-1</sup>).

14    Very good strong reliable fibre. Very stable.

15

16     **Example 12**

17	Na <sub>2</sub> O	36.68 mole %	
18	K <sub>2</sub> O	8.63 mole %	
19	P <sub>2</sub> O <sub>5</sub>	45.09 mole %	
20	B <sub>2</sub> O <sub>3</sub>	5.29 mole %	
21	Ag <sub>2</sub> O	2.59 mole %	
22	(CaO	1.73 mole %	to attenuate solution rate!

23

24    Furnace temperature 550°C.

25    Bushing 62 x 5.0mm holes.

26    Bushing temperature 400°C.

27    Speed 80kmph.

28    Very good fibres.

29    Solution rate 3.11 annealed, 3.8 non annealed (mg.cm<sup>-2</sup>.hr<sup>-1</sup>).

30

31    The fibres show excellent tensile strength, flexibility  
32    and shock resistance.

33

34    The fibres are especially suitable for industrial and  
35    plastics reinforcement controlled release (anti-  
36    microbial, anti-corrosion etc) and rapidly  
37    biodegradable applications.

38

39

**Example 13**

CaO 30 mole %  
MgO 20 mole %  
P<sub>2</sub>O<sub>5</sub> 50 mole %

Furnace at 1050°C.  
Bushing 5.5mm holes.  
Bushing temperature 700°C - 720°C.  
Speed up to 80kmph.  
Solution rate TBA.  
Very strong fibre.

**Example 14**

(K<sub>2</sub>O 5 mole %) Trace to alter dissolution rate  
CaO 25 mole %  
Mg<sub>2</sub>O 20 mole %  
P<sub>2</sub>O<sub>5</sub> 50 mole %

Furnace 1000°C.  
Bushing 5.5mm.  
Bushing temperature 560°C - 620°C.  
Speed up to 70kmph.  
Solution rate TBA.  
Very strong fibre.  
Anti-microbial.

**Example 15**

CaO 28.5 mole %  
MgO 18.5 mole %  
Ag<sub>2</sub>O 3 mole %  
P<sub>2</sub>O<sub>5</sub> 50 mole %

Furnace temperature 1050°C - 1150°C.  
Bushing 4 x 5.5mm.  
Bushing temperature 700°C.  
Speed 50kmph.  
Solution rate TBA.  
Very good, strong fibre.  
Anti-microbial.

1     **Example 16**

2	CaO	30 mole %
3	MgO	20 mole %
4	P <sub>2</sub> O <sub>5</sub>	50 mole %

5

6     As Example 15 (without silver)

7

8     The fibres show excellent tensile strength, flexibility  
9     and shock resistance. These fibres are suitable for  
10    applications requiring slower release and greater  
11    tensile strength plus biodegradability. The fibres are  
12    suitable for orthopaedic implants and tissue  
13    engineering applications.

14

15    **Example 17**

16    Producing a composite comprising soluble glass powder  
17    or granules.

18

19    Glass powder or granules can be added to the polymer to  
20    reinforce, stiffen or bulk the composite. The glass  
21    (for example based on the glasses of any of Examples 1  
22    to 16) can be used to release, for example,  
23    antimicrobials or trace elements. The glass, whose  
24    solution rate can be varied as required, reduces the  
25    volume of polymer to be degraded when used as a bulking  
26    agent.

27

28    The powder or granules/polymer composition can be made  
29    in various ways, as follows:

30

31    1.    Mixing the glass with solvent dissolved polymer,  
32          e.g. polycaprolactone can be dissolved in  
33          chloroform. Glass is added to the liquid and  
34          mixed. The solvent is evaporated to leave the  
35          composite.

36

37    2.    The glass can be mixed into melted polymer.

38

39    3.    The glass can be added to polymer masterbatch

1           which can then be used in extrusion or co-  
2           extrusion processes.

3

4       **Example 18**

5       Producing a composite comprising soluble glass fibre.

6

7       The addition of biodegradable glass fibre (as described  
8       in any of Examples 1 to 16) for reinforcement, bulking  
9       or controlled release in the polymer may be achieved by  
10       various methods, as follows:

11

12       1.     Fibre can be passed through a bath of polymer  
13               dissolved in solvent. The polymer solution can  
14               also be applied by passing the fibre over a  
15               rotating or counter-rotating transfer roller.

16

17       2.     Solvent dissolved polymer can be sprayed directly  
18               onto fibre as it is collected onto a drum or  
19               atomised into the jet attenuation venturi to  
20               produce coated wool.

21

22       3.     Continuous fibre can be fed through a bath of  
23               melted polymer.

24

25       4.     Fibre can be mixed into melted polymer or knitted  
26               or pre-formed into shapes to be layered into  
27               melted polymer. It may be possible to make sheets  
28               of polymer/fibre "sandwich" which can be thermally  
29               formed in a press.



## 1 CLAIMS

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

1. A biodegradable composite material suitable for implantation into a patient's body, said composite material comprising water-soluble glass and a biodegradable polymer.

2. The composite material as claimed in Claim 1, wherein said biodegradable polymer is a polyvinyl alcohol, polysaccharide, polyglycolic acid, polylactic acid, polyhydroxybutyrate, polyhydroxyvalerate, polycaprolactone, polycaprolactam or a starch.

3. The composite material as claimed in Claim 2 wherein said biodegradable polymer is poly  $\epsilon$ -caprolactone.

4. The composite material as claimed in any one of Claims 1 to 3 wherein said water-soluble glass is in the form of glass fibres and/or particles.

5. The composite material as claimed in any one of Claims 1 to 4 which comprises a matrix of water-soluble glass fibres and/or particles impregnated with said biodegradable polymer.

6. A method of repairing an area of defective tissue in a patient, said method comprising inserting the composite material as claimed in any one of Claims 1 to 5 into said patient in a quantity sufficient to cover and/or fill said area.

7. The method as claimed in Claim 6 wherein said tissue is nerve or bone.

8. The method as claimed in either one of Claims 6 and 7 wherein said composite material is attached to healthy tissue by suture and/or by

1 biodegradable adhesive.

2

3 9. A method of producing a composite material  
4 suitable for tissue repair, said method  
5 comprising:

6

7 a) providing water-soluble glass fibres and/or  
8 glass particles;

9 b) optionally arranging said fibres and/or  
10 particles into a pre-selected order;

11 c) covering said fibres and/or particles with a  
12 biodegradable polymer and if required allowing  
13 said polymer to cure.

14

15 10. The method as claimed in Claim 9 wherein said  
16 biodegradable polymer is poly  $\epsilon$ -caprolactone and  
17 wherein polymerisation occurs within the mould.

18

# INTERNATIONAL SEARCH REPORT

Internat'l Application No  
**PCT/GB 00/00475**

**A. CLASSIFICATION OF SUBJECT MATTER**  
**IPC 7 A61L27/58 A61L27/42 A61L27/46 A61L31/14 A61L31/12**

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
**IPC 7 A61L**

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 195 08 647 A (BIOVISION GMBH) 11 January 1996 (1996-01-11) claims	1,2,6-8
X	EP 0 146 398 A (SOUTHERN RES INST) 26 June 1985 (1985-06-26) page 4; claims	1-3,6,7
X	DATABASE WPI Section Ch, Week 199904 Derwent Publications Ltd., London, GB; Class A14, AN 1999-040635 XP002138589 & JP 10 298108 A (DAINIPPON INK & CHEM INC), 10 November 1998 (1998-11-10) abstract	1,2,6-8
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

**\* Special categories of cited documents :**

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the International search

**24 May 2000**

Date of mailing of the international search report

**07/06/2000**

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

**ESPINOSA, M**

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00475

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 169 914 A (MITSUBISHI MINING & CEMENT CO) 23 July 1986 (1986-07-23) claims; examples	1,2,4-7
X	WO 97 33632 A (GILTECH LTD ;GILCHRIST EILIDH (GB); GILCHRIST THOMAS (GB)) 18 September 1997 (1997-09-18) claims; examples 1-3	1,2
P,X	CORDEN T J ET AL: "Initial development into a novel technique for manufacturing a long fibre thermoplastic bioabsorbable composite: in-situ polymerisation of poly-epsilon-caprolactone" COMPOSITES PART A: APPLIED SCIENCE AND MANUFACTURING,NL,ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, vol. 30, no. 6, June 1999 (1999-06), pages 737-746, XP004164010 ISSN: 1359-835X page 738 page 745	1-10
P,X	WO 99 11296 A (BIONX IMPLANTS OY) 11 March 1999 (1999-03-11) claims; examples	1-10
A	US 4 604 097 A (KUMAR BINOD ET AL) 5 August 1986 (1986-08-05) claims	1-10
A	WO 98 44965 A (HEALY DAVID MICHAEL ;GILTECH LTD (GB)) 15 October 1998 (1998-10-15) claims	1-10

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00475

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19508647 A	11-01-1996	NONE	
EP 0146398 A	26-06-1985	US 4655777 A CA 1261991 A JP 60153868 A	07-04-1987 26-09-1989 13-08-1985
JP 10298108 A	10-11-1998	NONE	
GB 2169914 A	23-07-1986	JP 1471747 C JP 61135671 A JP 63019186 B CH 666281 A DE 3542535 A NL 8503340 A US 5013323 A	14-12-1988 23-06-1986 21-04-1988 15-07-1988 05-06-1986 01-07-1986 07-05-1991
WO 9733632 A	18-09-1997	AU 2032997 A CA 2247986 A EP 0888139 A	01-10-1997 18-09-1997 07-01-1999
WO 9911296 A	11-03-1999	AU 9622898 A	22-03-1999
US 4604097 A	05-08-1986	AU 5518386 A EP 0211942 A JP 7005335 B JP 62501905 T WO 8604807 A	10-09-1986 04-03-1987 25-01-1995 30-07-1987 28-08-1986
WO 9844965 A	15-10-1998	AU 6928598 A EP 0973562 A	30-10-1998 26-01-2000

**THIS PAGE BLANK (USPTO)**